

REMARKS

Claims 41-87 have been canceled. New Claims 88-134 have been added and are now active in this case.

REQUEST FOR RECONSIDERATION

Applicants wish to thank Examiner Hartley for the helpful and courteous discussion conducted with their U.S. representative on June 21, 2000. In accordance with the remarks made during the discussion, Applicants have modified the claims in order to clarify the present invention. Applicants now wish to make the following additional remarks.

As noted previously, in order to deliver drugs across the blood brain barrier of mammals, the conventional wisdom is that it is necessary to use nanoparticles to which drugs are complexed (incorporated or adsorbed) and which nanoparticles are surrounded by a coating made of an appropriate surfactant. See, for example, Kreuter et al (WO 95/22963), described at page 1 of the present specification. Quite surprisingly, it has now been discovered that effective nanosphere drug targeting systems can be provided, which do not require an outer coating of surfactant, and which can, therefore, be produced much more simply.

In particular, the present invention provides, in part, a drug targeting system for administration to a mammal, which contains:

a) nanoparticles made of a polymeric material, the nanoparticles being free of a surfactant surface coating and containing the polymeric material, one or more physiologically effective substances to be delivered to the mammal and one or more stabilizers for the nanoparticles allowing targeting of the physiologically effective substances to a specific site within or on a mammalian body;

wherein the stabilizers are selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12,000, carboxylic acid esters of glycerol, sorbitan monostearate, sorbitan monooleate, polyoxamer 188, polyoxamines, alkoxylated ethers, alkoxylated esters, alkoxylated mono-, di- and triglycerides, alkoxylated phenols and diphenols, the Genapol-based compounds, Bauki-based compounds, sodium stearate, metal salts of alcohol sulfates, metal salts of sulfosuccinates and mixtures of two or more of these substances; and

b) a physiologically acceptable carrier, which allows transport of the nanoparticles to the target within said mammal after administration.

Claims 41-83 stand rejected under 35 U.S.C. §102(b) as being anticipated by Hyon (EP 330180). However, this reference fails to either disclose or suggest the present invention.

In particular, and as noted previously, the emulsifying agents of Hyon are generally used to stabilize the emulsion therein, which is either an O/O type emulsion or a W/O type emulsion. That is, Hyon teaches the use of any conventional emulsifying agent as long as it is capable of forming a stable O/O or W/O type emulsion. Notably, this reference specifically teaches that:

For facilitating the formulation, an emulsifying agent is preferably employed. The emulsifying agent includes any conventional emulsifying agents insofar as they can form a stable O/O or W/O type emulsion . . . see page 5, lines 40-42.

For example, Example 1 at page 6 of Hyon teaches the use of "Span 80" as an emulsifier in the preparation of an emulsion. Attention is directed to page 1083 of Hawley's Condensed Chemical Dictionary (11th Edition) which defines "Span" as fatty acid partial esters of sorbitol anhydrides (or sorbitan).

Several comments are worthy of note.

First, Hyon clearly utilize a specific class of surfactants to produce an emulsion.

Hyon is not at all concerned with any medicinal effect arising from the use of the emulsifier in the subsequent dry formulation.

Second, although Applicants concede, as noted by the Examiner from page 4, lines 46-54 of Hyon, that the polymer nanoparticles of Hyon, themselves, may contain the "other pharmaceutically acceptable substances," it is emphasized that these other substances are necessarily "pharmaceutically acceptable" which means "inert" and having no effect on the active ingredients contained therewith.

Third, Hyon fails to disclose or suggest the specific stabilizers of the present invention. Notably, Hyon teaches specifically the possible use of polyoxyethylene sorbitan monolaurate. The term "monolaurate" denotes a monolaurate group which is a C₁₂ saturated group of the formula CH₃(CH₂)₁₀COO-.

In contrast, the closest convergence of the presently claimed stabilizers to this compound is 1) polysorbate 81 (polyoxyethylene sorbitan monoleate), wherein monoleate denotes the unsaturated C₁₇ group of the formula CH₃(CH₂)₇CH=CH(CH₂)₇COO-, 2) polysorbate 85 (polyoxyethylene sorbitan trioleate, denoting three of the above groups, and 3) sorbitan monoleate and sorbitan monostearate. Monostearate denotes the saturated C₁₈ group of the formula CH₃(CH₂)₁₆COO-. See Attachment 1 to this amendment and pages 685, 854 and 1091 of Hawley's, id.

Thus, it is clear that Hyon would fail to put one skilled in the art in possession of the present invention.

Finally, in view of Kreuter et al, discussed below, one skilled in the art would be taught to use a surfactant coating for nanoparticles in order to have the active ingredients contained therein cross the blood brain barrier. Thus, Kreuter et al teach away from the present invention.

Hence, this ground of rejection is unsustainable and should be withdrawn.

Claims 41-87 stand rejected under 35 U.S.C. §102(b) as being anticipated by Kreuter et al (WO 95/22963), Canal (EP 486959), Dyatlov (WO 94/15590) or Hyon (EP 330180).

However, none of these references, either alone or in combination, describes or suggests the present invention.

In particular, Kreuter et al, as noted at page 1 of the present specification, necessarily teach the use of a surfactant coating on the nanoparticles thereof. Quite clearly, the present invention avoids the use of the surfactant coating. In fact, one of the principle objects of the present invention is the avoidance of such a surfactant surface coating on the nanoparticles.

Notably, Kreuter et al describe the preparation of nanoparticles "in conventional ways". See the Abstract. The nanoparticles are "then coated with additional surfactant and given to the body of animals or humans". See the Abstract. Thus, the nanoparticles of this reference are clearly characterized by the presence of an outer coating of surfactant.

Moreover, the stated reason for using this outer coating of surfactant is to allow "drugs or diagnostic agents to cross the blood-brain barrier (bbb)". See the Abstract. Kreuter et al describe the many conventional approaches which have been used to allow administered drugs to cross the blood-brain barrier. See pages 2-5 thereof. In contrast thereto, Kreuter et al teach that their invention:

... is based on the surprising finding that treatment of nanoparticles having a drug absorbed, adsorbed or incorporated therein with a sufficient coating of an appropriate surfactant allows the adsorbed drug to traverse the bbb. See page 6 thereof.

Further, Kreuter et al teach that:

The critical, innovative step is that after drug absorption or incorporation, the nanoparticles are coated with surfactants by incubating them in a surfactant solution under appropriate

conditions. The surfactant allows penetration of the bbb by the drug without physical modification of the nanoparticle or the drug itself. See page 7 thereof.

In contrast, the present invention surprisingly avoids the use of the outer coating of surfactant as taught by Kreuter et al. See pages 3 and 4 of the present specification. Clearly, in view of the teachings of Kreuter et al., one skilled in the art would have no motivation to avoid the use of the outer coating of surfactant, as without the coating, one skilled in the art would not expect administered drugs to cross the blood-brain barrier as in the present invention.

Furthermore, the particular stabilizers used in accordance with the present invention are readily distinguishable from the substances used in Dyatlov et al and Canal et al. Notably, the present invention uses specific stabilizers which are neither disclosed nor suggested by either of these cited references.

Further, the emulsifying agents of Hyon et al are merely used to stabilize the emulsion therein, which is either a O/O type emulsion or a W/O type emulsion. That is, Hyon et al clearly teach the use of any conventional emulsifying agent insofar as they are able to form a stable O/O or W/O type emulsion. Thus, the stabilizer of Hyon et al is a stabilizer of the emulsion and is clearly not incorporated into a nanoparticle. In contrast, the stabilizer of the present invention is incorporated into the polymer of the nanoparticle for stabilization in order to obtain the desired targeting of the nanoparticles to or on specific targets in or on the mammalian body without using the outer surfactant coating of Kreuter et al.

Quite clearly, one skilled in the art would not be put in possession of the present invention even from the combined teachings of these references.

Hence, this ground of rejection is believed to be unsustainable and should be

withdrawn.

Claims 48, 68 and 70 stand rejected under 35 U.S.C. §112, first paragraph.

However, in view of the above amendments, this ground of rejection is believed to be moot.

Claims 41, 50, 48, 54, 55, 68, 70 and 72 stand rejected under 35 U.S.C. §112, second paragraph.

However, in view of the above amendments, this ground of rejection is believed to be moot.

Also, Applicants attach to this response page 36, of the original application, containing an Abstract, which appears to be missing from the Official Patent Office file.

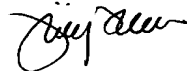
Applicants also respectfully assert that diagnostic substances used in nuclear medicine and radiation therapy are well known to those skilled in the art. Hence, it is respectfully submitted that Claims 97, 119 and 120 are proper.

Finally, also attached to this amendment, is a list of generic chemical definitions for the terms queried by the Examiner.

Accordingly, in view of all of the above amendments and attendant remarks, it is believed that the present application now stands in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

William E. Beaumont
Registration No. 30,996



22850

(703) 413-3000
Fax #: (703) 413-2220
NFO/WEB:cct/pae

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IN THE CLAIMS

Claims 41-87 (Canceled)

Claims 88-134 (New)

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lattice. (1) The structural arrangement of atoms in a crystal. Accurate information is obtained by x-rays, which are diffracted by the lattice at various angles. As the atoms are from 1.5–3 Å apart in most crystals, the lattice acts as a diffraction grating. See also crystals, dislocation. (2) The array of nuclear fuel elements and moderator in a nuclear reactor.

"Latyl."²⁸ TM for a group of disperse dyes developed particularly for coloration of "Dacron" polyester fiber, on which they have exceptionally good light and wet fastness properties.

laudanidine. (levo-laudanine; tritopine).

CAS: 301-21-3. $C_{20}H_{25}O_4N$. Analkaloid.

Properties: White crystals, mp 182–185°C. Insoluble in water; soluble in alcohol, benzene, chloroform, and slightly soluble in ether.

Derivation: From opium.

Hazard: Toxic by ingestion.

Use: Medicine (analgesic).

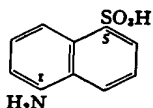
laudanum. Tincture of opium (tinctura opii BP).

laughing gas. See nitrous oxide.

laundry sour. See sour.

lauraldehyde. See lauryl aldehyde.

Laurent's acid. (1-naphthylamine-5-sulfonic acid).



Properties: White or pink needles, gives greenish fluorescence in dilute aqueous solution.

Derivation: From naphthalene- α -sulfonic acid by nitration, reduction with iron, and separation from the 1-naphthylamine-8-sulfonic acid also formed.

Use: Azo dye intermediates.

Laurent's α acid. (1-nitronaphthalene-5-sulfonic acid). $C_{10}H_6(NO)_2(SO_3H)$.

Properties: Pale yellow needles, soluble in water, alcohol and ether. Combustible.

Derivation: By sulfonating nitronaphthalene with a mixture of chlorohydrin and sulfuric acid.

Use: Dye intermediate.

"Laurex."²⁴⁸ TM for the zinc salts of a mixture of fatty acids in which lauric acid predominates.

Properties: Yellowish white granulated waxy powder, d 1.15, mp 95–105°C. Soluble in benzene;

insoluble in acetone, gasoline, ethylene dichloride, and water. Combustible.

Use: Accelerator, activator, and plasticizer for rubber.

lauric acid. (dodecanoic acid).

CAS: 143-07-7. $CH_3(CH_2)_{10}COOH$.

A fatty acid occurring in many vegetable fats as the glyceride, especially in coconut oil and laurel oil. Combustible.

Properties: Colorless needles, d 0.833, mp 44°C, bp 225°C (100 mm), refr index 1.4323 (45°C), insoluble in water, soluble in benzene and ether.

Derivation: Fractional distillation of mixed coconut or other acids.

Grade: 99.8% pure, technical, FCC.

Use: Alkyd resins, wetting agents, soaps, detergents, cosmetics, insecticides, food additives.

lauric aldehyde. See lauryl aldehyde.

laurone. An aliphatic ketone, insoluble in water, stable to high temperatures, acids, alkalis. Compatible with high-melting vegetable waxes, fatty acids, paraffins, etc. Incompatible with resins, polymers and organic solvents at room temperature, but compatible with them at high temperature.

Use: As antilock agent.

N-lauroyl-p-aminophenol.

$HO(C_6H_4)NHCOCH_2(CH_2)_9CH_3$.

Properties: White to off-white powder; mp 123–126°C; insoluble in water; soluble in polar organic solvents (especially when heated) including alcohol, acetone, and dimethylformamide.

Use: Rubber antioxidant.

lauroyl chloride. $C_{11}H_{23}COCl$.

Properties: Water-white liquid, refr index 1.445 (20°C), fp –17°C, bp 145°C (18 mm), decomposes in water and alcohol, soluble in ether.

Use: Surfactant, polymerization initiator, antienzyme agent, foamer; synthesis of lauroyl peroxide, sodium-N-lauroyl sarcosinate, and other sarcosinates.

lauroyl peroxide. (dodecanoyl peroxide).

CAS: 105-74-8. $(C_{11}H_{23}CO)_2O_2$.

Properties: White, coarse powder; tasteless; faint odor. Soluble in oils and in most organic solvents, slightly soluble in alcohols, insoluble in water, mp 49°C.

Grade: Technical (about 95%).

Hazard: Dangerous fire and explosion risk, will ignite organic materials, strong oxidizer. Toxic by ingestion and inhalation, strong irritant to skin.

Use: Bleaching agent, intermediate and drying

Properties: Ivory-colored powder, mp 72C, d 0.94. Combustible.

Grade: Refined.

Use: Slip-agent for extrusion of polyethylene, wax additive, ink additive.

olefin. (alkene). A class of unsaturated aliphatic hydrocarbons having one or more double bonds, obtained by cracking naphtha or other petroleum fractions at high temperatures (1500–1700F). Those containing one double bond are called alkenes, and those with two alkadienes, or diolefins. They are named after the corresponding paraffins by adding “-ene” or “-ylene” to the stem. α -olefins are particularly reactive because the double bond is on the first carbon. Examples are 1-octene and 1-octadecene, which are used as the starting point for medium-biodegradable surfactants. Other olefins (ethylene, propylene, etc.) are starting points for certain manufactured fibers.

See also: diolefin.

oleic acid. (cis-9-octadecenoic acid; red oil).

CAS: 112-80-1.

$\text{CH}_3(\text{CH}_2)_7\text{CH}:\text{CH}(\text{CH}_2)_7\text{COOH}$. A mono-unsaturated fatty acid, a component of almost all natural fats as well as tall oil. Most oleic acid is derived from animal tallow or vegetable oils.

Properties: Commercial grades: Yellow to red oily liquid; lard-like odor; darkens on exposure to air. Insoluble in water; soluble in alcohol, ether, and most organic solvents; fixed and volatile oils. Solvent for other oils, fatty acids and oil-soluble materials. Purified grades: Water-white liquid, d 0.895 (20/4C); bp 14C, bp 286C (100 mm); 225C (10 mm); refr. index 1.4599 (20C); acid value 196–204; iodine value 83–103; saponification value 196–206; flash p 372 (189C). Combustible. Derivation: The free fatty acid is obtained from the glyceride by hydrolysis, steam distillation and separation by crystallization or solvent extraction. Filtration from the press cake results in the oleic acid of commerce (red oil), which is purified and bleached for specific uses. Grade: Variety of technical grades, grade free from chick edema factor, USP, FCC, 99+%. A purified technical oleic acid containing 90% or more oleic, 4% maximum linoleic and 6% maximum saturated acids is available.

Use: Soap base, manufacture of oleates, ointments, cosmetics, polishing compounds, lubricants, ore flotation, intermediate, surface coatings, food-grade additives.

olein. (triolein; glyceryl trioleate).

$(\text{C}_{17}\text{H}_{33}\text{COO})_3\text{C}_3\text{H}_5$. The triglyceride of oleic

acid, occurring in most fats and oils. It constitutes 70–80% of olive oil.

Properties: Yellow, oily liquid; d 0.915; mp –4 to –5C; soluble in chloroform, ether, carbon tetrachloride; slightly soluble in alcohol. Combustible. Impurities: Stearin, linolein.

Derivation: Refined natural oils.

Use: Textile lubricants.

oleoresin. Any of a number of mixtures of essential oils and resins characteristic of the tree or plant from which they are derived. Most types are semisolid and tacky at room temperature, becoming soft and sticky at high temperatures. They have various distinctive odors.

See also: balsam, rosin.

oleoyl chloride. (cis-9-octadecenoyl chloride).

$\text{CH}_3(\text{CH}_2)_7\text{CH}:\text{CH}(\text{CH}_2)_7\text{COCl}$.

Properties: Liquid, bp 175–180C (3 mm), soluble in hydrocarbons and ethers, reacts slowly with water. Combustible.

Use: Chemical intermediate.

n-oleoylsarcosine.

$\text{C}_{17}\text{H}_{33}\text{C}(\text{O})\text{N}(\text{CH}_3)\text{CH}_2\text{COOH}$.

Properties: Amber liquid, d 0.955 (20/20C), refr. index 1.4703 (20C), 95% pure. Combustible.

Use: Surfactants.

oleum. The Latin word for oil, applied to fuming sulfuric acid. (Sulfuric acid was originally called oil of vitriol).

oleyl alcohol. (octadecenol). CAS: 143-28-2.

$\text{CH}_3(\text{CH}_2)_7\text{CH}:\text{CH}(\text{CH}_2)_7\text{CH}_2\text{OH}$. The unsaturated alcohol derived from oleic acid. Clear, viscous liquid at room temperature. Iodine value 88, cloud p –6.6C, bp 333C, fp –75C, d 0.84. Combustible. Impurities: Linoleyl, myristyl, and cetyl alcohols.

Derivation: Reduction of oleic acid, occurs in fish and marine mammal oils.

Grade: Technical, commercial (80–90% pure).

Use: Surfactants, metal cutting oils, printing inks, textile finishing, antifoam agent, plasticizer.

oleyl aldehyde. See octadecenyl aldehyde.

oleylhydroxamic acid. $\text{C}_{17}\text{H}_{33}\text{CONHOH}$.

Properties: Waxy solid, off-white color, d 0.897 (70/25C), insoluble in water; soluble in aqueous potassium hydroxide and organic solvents.

oleyl-linoleylamine. (octadecene-octadecadienamine).

Properties: Highly unsaturated primary amine,

unique types of chemical reactions occur in outer space, and that actual products may result that are not achievable under terrestrial environment. Several factors are believed to account for this, primarily zero gravity, though absence of oxygen and enhanced magnetic effects may also play a part. Several encouraging results have already been obtained, though until further experiments and operating data have been investigated the conclusions must be considered tentative. Among projects that have been carried out or are contemplated are the following: (1) Uniform polymer microspheres that are over twice as large as possible on earth have been made due to zero gravity. (2) More effective electrophoresis reactions for making biological materials have been discovered, probably also because of zero gravity. (3) Possibilities exist for (a) making unique alloys in space that are not possible on earth, for example lead-copper, lead-zinc, and aluminum-indium; (b) purer crystals for microelectronics; (c) better glass for fiber optics; (d) new drugs and pharmaceuticals. Future experiments will involve human cells, enzymes, and hormones.

space velocity. The volume of gas or liquid, measured at specified temperature and pressure (usually standard conditions) passing through unit volume in unit time.

Use: Comparing flow processes involving different conditions, rates of flow and sizes or shapes of containers.

spalling. Chipping an ore for crushing, or the cracking, breaking, or splintering of materials due to heat.

"Span."⁸⁹ TM for each member of a series of general-purpose emulsifiers and surface-active agents. They are fatty acid partial esters of sorbitol anhydrides (or sorbitan). Generally insoluble in water and soluble in most organic solvents.

spandex. Generic name for a fiber in which the fiber-forming substance is a long-chain synthetic polymer comprised of at least 85% of a segmented polyurethane (Federal Trade Commission). Imparts elasticity to garments such as girdles, socks, special hosiery.

spanish white. (1) chalk, CaCO_3 ; (2) bismuth white, $\text{BiO}(\text{NO}_3)$, basic bismuth white.

spar. (1) A type of crystalline material such as Iceland spar or feldspar, usually containing calcium carbonate or an aluminum silicate; fluor-spar is calcium fluoride. Iceland spar has unique optical properties. (2) A weather-resistant varnish originally used for coating wooden decks

of ships, which may be the reason for its name. See spar varnish.

sparger. A perforated pipe through which steam, air or water is sprayed into a liquid during a fermentation reaction.

Use: Brewing industry to remove traces of wort from the mash.

spar, Greenland. See cryolite.

spar, heavy. See barite.

spar, Iceland. See calcite.

sparking metal. See pyrophoric alloy.

spar, satin. See calcite; gypsum.

spar varnish. A durable, water-resistant varnish for severe service on exterior exposure. It consists of one or more drying oils (linseed, tung, or dehydrated castor oil), one or more resins (rosin, ester gum, phenolic resin, or modified phenolic resin), one or more volatile thinners (turpentine or petroleum spirits), and driers (linoleates, resinates, or naphthenates of lead, manganese, and cobalt). It is classed as a long-oil varnish and generally consists of 45–50 gals of oil for each 100 lb of resin.

See also varnish.

SPE. Abbreviation for Society of Plastics Engineers.

spearmint oil. A yellowish essential oil, strongly levorotatory.

Use: Source of carvone and as flavoring for medicines, chewing gum, etc.

specification. A schedule of minimum performance requirements for specialized products such as those established by the various committees of the American Society for Testing and Materials and the Underwriters Laboratories. Such products are subject to inspection and test before acceptance.

See also testing.

specific gravity. The ratio of the density of a substance to the density of a reference substance; it is an abstract number that is unrelated to any units. For solids and liquids, specific gravity is numerically equal to density, but for gases it is not, because of the difference between the densities of the reference substances, which are usually water (1 g/cc) for solids and liquids and air (0.00129 g/cc, or 1.29 g/L at 0°C and 760 mm) for gases. The specific gravity of a gas is the

bleached. They act as emulsifiers, stabilizers, antioxidants.

Use: Foods, especially chocolate and compound coatings, candies, bakery products, margarine, industrial uses; paints and printing inks, soaps and cosmetics, textile compounds, leather tanning, petroleum lubricants; animal feeds and pet foods.

"Sta-Tac."³⁶ TM for olefinic hydrocarbon resins used as coating vehicles.

"Stat-Eze."⁴³⁰ TM for a specially prepared quaternary ammonium compound.

Use: Externally applied antistatic agent on plastics, textiles, paper, and carpeting.

Staudinger, Hermann. (1881-1965) A German chemist, winner of a Nobel Prize in 1953 for his pioneer work on the structure of macromolecules and polymerization. A large part of modern high-polymer chemistry is based on his original research.

Staudinger reaction. Synthesis of phosphazo compounds by the reaction of tertiary phosphines with organic azides.

"Staybelite."²⁶⁶ TM for hydrogenated rosin, a pale, thermoplastic resin. Acid number 165, USDA color X, softening point 75C, saponification number 167.

Use: Adhesives and protective coatings.

"Stayco."⁴⁹² TM for a family of oxidized starches. Available in five viscosities: S, A, G, C, and M.

Use: Paper industry for wet-end addition, in tub, press, and calender sizing, and as coating adhesives.

"Stayrite."¹⁰⁴ TM for stabilizers used to provide increased heat and light stability to vinyl resins. Available in range of products, both liquid and solid.

"Staysize" 109.⁴⁹² TM for a white, highly uniform, chemically modified corn starch in pearl form developed for surface sizing.

"Stayzyme."⁴⁹² TM for a thick-boiling corn starch buffered to a pH of 6.3-7.0 to produce the proper pH for enzyme conversion in the paper mill.

steam. An allotropic form of water formed at 212F (100C) and having a latent heat of condensation of 540 calories per gram. It has a number of industrial uses, one of the most important be-

ing the production of hydrogen by the steam-hydrocarbon gas process (reforming), by the steam-water gas process, the steam-iron process, and the steam-methanol process. It is also used in steam cracking of gas oil and naphtha; in food processing, as a cleaning agent; in rubber, vulcanization; as a source of heat and power; in distillation of plants for production of essential oils and perfumes; and in secondary oil recovery.

Steam from geothermal sources such as hot springs and fumaroles is utilized as an energy source. Steam for industrial processing is also being generated by solar energy techniques. See geothermal energy, latent heat.

steam distillation. See hydrodistillation.

steam reforming. See reforming.

steapsin. A lipase in the pancreatic juice. See enzyme.

stearamide. (octadecanamide).

CAS: 124-26-5. $\text{CH}_3(\text{CH}_2)_{16}\text{CONH}_2$.

Properties: Colorless leaflets, mp 109C, bp 251C (12 mm), insoluble in water, slightly soluble in alcohol and ether.

Use: Corrosion inhibitor in oil wells.

stearato chromic chloride. A polynuclear complex in the form of a six-membered ring. The two chromium atoms are bridged on one side by a hydroxyl group, and on the other side by the carboxyl oxygens of the stearic acid. The water-soluble complex results from the neutralization of stearic acid with basic chromic chloride. It acts as a water repellent and abherent.

stearic acid. (n-octadecanoic acid).

CAS: 57-11-4. $\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$.

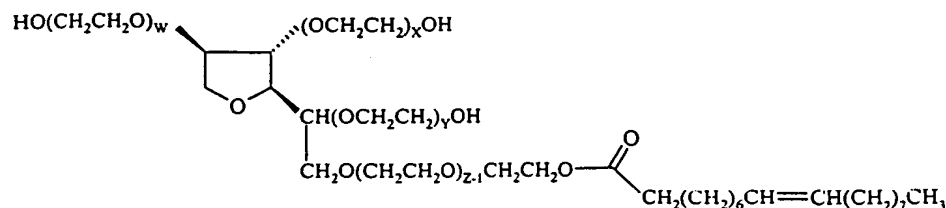
The most common fatty acid occurring in natural animal and vegetable fats. Most commercial stearic acid is 45% palmitic acid, 50% stearic acid and 5% oleic acid, but purer grades are increasingly used.

Properties: Colorless, wax-like solid; odor and taste slight suggesting tallow. Soluble in alcohol, ether, chloroform, carbon disulfide, carbon tetrachloride; insoluble in water. D 0.8390 (80/4C), mp 69.6C, bp 361.1C, refr index 1.4299 (80C), flash p 385F (196C), autoign temperature 743F (395C). Combustible.

Derivation: (a) From high-grade tallows and yellow grease stearin by washing, hydrolysis with the Twitchell or similar reagent, boiling, distilling, cooling, and pressing; (b) from oleic acid by hydrogenation.

Grade: Saponified, distilled, single-pressed, double-pressed, triple-pressed, USP, FCC, 90%

Structure of "Polysorbate 80" (= Tween^R 80) (see "R")



$$W + X + Y + Z = 80$$

There are also existing Polysorbate (= Tween^R) 20, 21, 40, 60, 61, 65, 81, 85.

Examples: Polysorbate 81 (= Tween^R 81): Polyoxyethylene sorbitan monooleate
 Polysorbate 85 (= Tween^R 85): Polyoxyethylene sorbitan trioleate

Structure of "Genapol C" 100 (see "R")

$\text{CH}_3(\text{CH}_2)_y-(\text{OCH}_2\text{CH}_2)_x-\text{OH}$ = Polyetheleneglycol(10) laurylether

There are also existing Genapol X-080, Genapol X-100 and Genapol X-150.

Structure of Poloxamer (= Pluronic^R) F 68 (see "R")

$\text{HO}-(\text{CH}_2\text{CH}_2\text{O})_x (\text{CH}(\text{CH}_3)\text{CH}_2\text{O})_y (\text{CH}_2\text{CH}_2\text{O})_z\text{H}$

= Polyethyleneglycol polypropyleneglycol copolymer

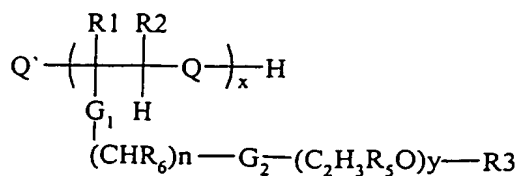
There are also existing Poloxamer (= Pluronic^R) F-108 and F-127.

Structure of the BAUKI surfactants (see U.S. Patent No. 5,576,012)

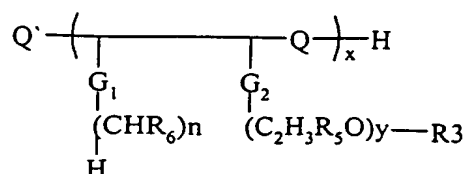
These surfactants are named according to the family names of the two German inventors Kurt H. BAUer and Markus Kiefer.

There are existing two general formulae, namely

I.



II.



wherein

R1, R2, R5 and R6 may be identical or different and have the meaning of H, methyl or ethyl;

R3 is H or a lower alkyl group having 1 to 6 carbon atoms;

Q may either be a direct bond or – O – or an ester functional group or an amide functional group;

Q' may be H, if Q is a direct bond or – O –, or Q' is –OH or an amino group, if Q is an ester functional group or an amide functional group;

x may have values in the range of from 3 to 50, preferably in the range of from 5 to 40, if Q is a direct bond or – O –, or x may have values in the range of from 3 to 1000, preferably in the range of from 50 to 100, if Q is an ester functional group or an amide functional group;

G1 and G2 may be identical or different and may be a direct bond, - O -, an ester functional group or an amide functional group;

n may have values in the range of from 4 to 44, preferably in the range of from 12 to 16; and

y may have values in the range of from 2 to 50, preferably in the range of from 10 to 40.